AMENDMENTS TO THE CLAIMS

1. (currently amended) A recombinant chimer hepatitis B core (HBc) protein molecule up to about 600 amino acid residues in length that

(a) contains an HBc sequence of at least about 125 of the N-terminal 183 amino acid residues of the HBc molecule that includes the HBc sequence of residue positions 4 through about 75 and about 85 through about 140 in which one or both cysteine residues at positions 48 and 107 is replaced by another residue, and in which the cysteine at residue position 61 is present;

(b) contains a peptide-bonded heterologous amino acid residue sequence at one or more of the N-terminus, in the HBc immunodominant loop between residue positions about 76 through about 85 or the C-terminus of the chimer, and wherein

[(i)] (1) zero to all residues in a sequence in said HBc immunodominant loop are present or replaced and said heterologous amino acid residue sequence comprises one to about 245 amino acid residues that constitute an immunogen or a sequence of 1 to about 40 residues that constitutes an anti-antigen or a chemically-reactive linker residue for a conjugated hapten; or

[(ii)] (2) the sequence of HBc at positions 76 through 85 is present and free from deletions and heterologous residues; or

[(iii)] (3) one or more of residues 76 through 85 is absent or replaced;

(c) contains one or both of

[(i)] (1) one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the

HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence and

[(ii)] (2) one to three cysteine residues toward the C-terminus of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)]; said chimer molecule

(i) containing up to about 5 percent substituted amino acid residues in the HBc sequence relative to SEQ ID NO:1, and

(ii) self-assembling into particles that exhibit a ratio of absorbance at 280 nm to 260 nm of about 0.9 to about 1.7 after expression.

2. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 wherein the N-terminal sequence includes a heterologous sequence containing up to about 75 amino acid residues peptide-bonded to one of HBc residues 2-4 that includes an immunogenic epitope.

3. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 wherein the sequence of HBc at position about 76 through about 85 is present and free from deletions and heterologous residues.

4. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 wherein zero to all residues in a sequence of HBc positions 76 through 85 are present and peptide-bonded to one to about 245 amino acid residues that are heterologous to HBc and constitute a heterologous epitope.

5. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 wherein one or more of residues 76 through 85 is absent or replaced.

6. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 wherein the C-terminal sequence contains up to about 100 amino acid residues that include an immunogenic epitope in a sequence heterologous to HBc and bonded to said C-terminal residue of the HBc sequence.

7. (original) The recombinant chimer hepatitis B core (HBc) protein molecule according to claim 1 wherein the HBc residue at each of positions 76 and 82 is replaced by a cysteine residue.

8. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 that contains an HBc sequence of at least about 125 of the N-terminal 163 amino acid residues of the HBc molecule.

9. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 that is up to about 380 amino acid residues in length.

10. (original) The recombinant chimer hepatitis B core protein molecule according to claim 1 that contains at least about 135 of the N-terminal 163 amino acid residues of HBc.

11. (previously presented) A recombinant chimer hepatitis B core (HBc) protein molecule up to about 380 amino acid residues in length that

(a) contains an HBc sequence of at least about 125 of the N-terminal 163 amino acid residues of the HBc molecule that includes the HBc sequence of residue positions 4 through about 75 and about 85 through about 140 in which one or both cysteine residues at positions 48 and 107 is replaced by another residue, and in which the cysteine at residue position 61 is present;

(b) includes one or more of the following:

(i) a peptide-bonded heterologous sequence of up to about 75 residues at one or more of the N-terminus, in the HBc immunodominant loop and at the C-terminus of the chimer wherein that C-terminal sequence is other than that of HBc from position 163 through the native HBc C-terminus,

(ii) zero to all of the residues of the sequence of position about 76 through about 85 are present or replaced , wherein

(iia) said heterologous sequence of up to about 75 amino acid residues is peptide-bonded to the sequence between about positions 76 through about 85, or

(iib) a sequence of one to about 40 amino acid residues that constitute an anti-antigen is peptide-bonded to the sequence between about positions 76 through about 85, or

(iic) a chemically-reactive linker residue for a conjugated hapten is peptide-bonded to the sequence between about positions 76 through about 85, or

(iid) the sequence of HBc at position about 76 through about 85 is present and free from deletions and heterologous residues, or

(iie) one or more of residues about 76 through about 85 is absent or replaced;

(c) contains one to three cysteine residues present

(i) at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence, or

(ii) toward the C-terminus of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)], or at both locations (i) and (ii);

(d) contains up to about 5 percent substituted amino acid residues in the HBc sequence relative to SEQ ID NO:1, and

(e) self-assembles into particles after expression that upon collection, purification and dissolution, exhibit a ratio of absorbance at 280 nm to 260 nm of about 0.9 to about 1.7.

12. (original) The recombinant chimer hepatitis B core protein molecule according to claim 11 that contains one to three C-terminal cysteine residue(s).

13. (original) The recombinant chimer hepatitis B core protein molecule according to claim 11 that contains at least about 135 of the N-terminal 163 amino acid residues of HBc.

14. (original) The recombinant chimer hepatitis B core protein molecule according to claim 13 that contains an HBc

sequence of at least about 135 of the N-terminal 156 amino acid residues of the HBc molecule.

15. (original) The recombinant chimer hepatitis B core (HBc) protein molecule according to claim 11 wherein the residue of HBc at each of positions 76 and 82 is replaced by a cysteine residue.

16. (original) The recombinant HBc chimer protein molecule according to claim 11 wherein said peptide-bonded sequence of up to about 75 residues is present.

17. (original) The recombinant HBc chimer protein molecule according to claim 16 wherein said peptide-bonded sequence of up to about 75 residues is present bonded at the N-terminus of the chimer.

18. (original) The recombinant HBc chimer protein molecule according to claim 16 wherein said peptide-bonded sequence of up to about 75 residues is present bonded in the HBc immunodominant loop of the chimer.

19. (original) The recombinant HBc chimer protein molecule according to claim 16 wherein said peptide-bonded sequence of up to about 75 residues is present bonded at the C-terminus of the chimer.

20. (original) The recombinant HBc chimer protein molecule according to claim 16 that contains a second peptide-bonded sequence of up to about 75 residues present bonded to the N-terminus, in the HBc immunodominant loop or to the C-terminus

of the chimer at a position different from that to which the first-named sequence of up to about 75 residues was bonded.

21. (original) The recombinant HBc chimer protein molecule according to claim 20 wherein said first-named sequence of up to about 75 residues contains a B cell epitope.

22. (original) The recombinant HBc chimer protein molecule according to claim 21 wherein said second-named sequence of up to about 75 residues contains a T cell epitope.

23. (original) The recombinant HBc chimer protein molecule according to claim 11 wherein both cysteine residues at positions 48 and 107 are replaced by another residue.

24. (original) The recombinant HBc chimer protein molecule according to claim 23 wherein the replacement residue for each cysteine is selected from the group consisting of glutamine, asparagine, serine, alanine, threonine and lysine.

25. (currently amended) A recombinant hepatitis B virus core (HBc) protein chimer molecule that has a length of about 135 to about 365 amino acid residues and contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

Domain I comprises about 72 to about 150 amino acid residues whose sequence includes:

[(i)] (a) at least the sequence of the residues of position 4 through position 75 of HBc,

[(ii)] (b) the substitution of another residue for the cysteine residue at position 48, while maintaining the cysteine at residue position 61,

[(iii)] (c) zero to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence, and

[(iv)] (d) an optional immunogenic epitope sequence containing up to about 75 amino acid residues peptide-bonded to one of HBc residues 2-4;

Domain II comprises up to about 60 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which those peptide-bonded amino acid residues comprise

(a) the sequence of 10 residues of HBc positions 76 through 85 present, but interrupted by

[(i)] (1) one to about 50 residues of a heterologous immunogen-containing sequence, or

[(ii)] (2) 1 to about 40 residues of an anti-antigen-containing sequence, or

[(iii)] (3) 1 to about 40 residues of a sequence containing a chemically-reactive linker residue for a conjugated hapten, or

(b) the sequence of HBc positions 76-85 is present with two replacement cysteine residues at HBc positions 76 and 82, and includes an interrupting sequence of

[(i)] (1) up to 50 residues of a heterologous immunogen-containing sequence, or

[(ii)] (2) 1 to about 40 residues of an anti-antigen-containing sequence; or

[(iii)] (3) 1 to about 40 residues of a sequence containing a chemically-reactive linker residue for a conjugated hapten;

Domain III comprises an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II in which another residue is substituted for the cysteine of position 107;

Domain IV comprises:

[(i)] (a) five through about thirty residues of an HBc amino acid residue sequence from position 136 through about 165 peptide-bonded to the residue of position 135 of Domain III,

[(ii)] (b) zero to three cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the C-terminus of the chimer molecule,

[(iii)] (c) zero to about 75 amino acid residues in a sequence other than that present in HBc from position 165 to the C-terminus, and the sequence of the chimer molecule from HBc position 150 through the C-terminus of the chimer molecule contains fewer than about ten arginine or lysine residues or mixtures of both residues; said chimer molecule

(i) having an amino acid residue sequence in which up to about 5 percent of the amino acid residues are substituted in the HBc sequence of the chimer relative to SEQ ID NO:1,

(ii) having at least one cysteine residue present from the recited zero to three cysteine residues of Domains I and IV, and

(iii) self-assembling into particles on expression by a host cell wherein the particles so formed exhibit a ratio of absorbance at 280 nm to 260 nm of about 0.9 to about 1.7 and are more stable by size exclusion

chromatography after storage at 37° C in a 20 mM sodium phosphate buffer at pH 6.8 for a time period of one month than are particles formed from otherwise identical HBc chimer molecules that contain both cysteine residues at positions 48 and 107.

26. (original) The recombinant chimer hepatitis B core protein molecule according to claim 25 that contains one to three C-terminal cysteine residue(s).

27. (original) The recombinant chimer hepatitis B core protein molecule according to claim 25 that contains at least about 135 of the N-terminal 156 amino acid residues of HBc.

28. (original) The recombinant chimer hepatitis B core protein molecule according to claim 27 that contains an HBc sequence of at least about 135 of the N-terminal 149 amino acid residues of the HBc molecule.

29. (original) The recombinant chimer hepatitis B core protein molecule according to claim 25 wherein the residue of HBc at each of positions 76 and 82 is replaced by a cysteine residue.

30. (original) The recombinant HBc chimer protein molecule according to claim 25 wherein a peptide-bonded sequence of up to about 75 residues is present.

31. (original) The recombinant HBc chimer protein molecule according to claim 30 wherein said peptide-bonded

sequence of up to about 75 residues is present bonded at the N-terminus of the chimer.

32. (original) The recombinant HBc chimer protein molecule according to claim 30 wherein said peptide-bonded sequence of up to about 75 residues is present bonded in the HBc immunodominant loop of the chimer.

33. (original) The recombinant HBc chimer protein molecule according to claim 30 wherein said peptide-bonded sequence of up to about 75 residues is present bonded at the C-terminus of the chimer.

34. (original) The recombinant HBc chimer protein molecule according to claim 30 that contains a second peptide-bonded sequence of up to about 75 residues present bonded to the N-terminus, in the HBc immunodominant loop or to the C-terminus of the chimer at a position different from that to which the first-named sequence of up to about 75 residues was bonded.

35. (original) The recombinant HBc chimer protein molecule according to claim 34 wherein said first-named sequence of up to about 75 residues contains a B cell epitope.

36. (original) The recombinant HBc chimer protein molecule according to claim 35 wherein said B cell epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 5 residues of the HBc sequence of positions 76 through 85 are present.

37. (original) The recombinant HBc chimer protein molecule according to claim 36 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said B cell epitope.

38. (original) The recombinant HBc chimer protein molecule according to claim 35 wherein said second-named sequence of up to about 75 residues contains a T cell epitope.

39. (original) The recombinant HBc chimer protein molecule according to claim 38 wherein said T cell immunogenic epitope is peptide-bonded to the C-terminal HBc amino acid residue.

40. (original) The recombinant HBc chimer protein molecule according to claim 39 wherein at least one of said C-terminal cysteine residue(s) is present.

41. (original) The recombinant HBc chimer protein molecule according to claim 25 wherein said chimer contains the uninterrupted HBc amino acid residue sequence of position 4 through at least position 140, plus a cysteine residue at the C-terminus of the HBc chimer protein molecule.

42. (original) The recombinant HBc chimer protein molecule according to claim 41 wherein said chimer contains the uninterrupted HBc amino acid residue sequence of position 4 through position 149.

43. (original) The recombinant HBc chimer protein molecule according to claim 25 wherein said chimer contains a

heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop.

44. (original) The recombinant HBc chimer protein molecule according to claim 43 wherein said heterologous linker residue for a conjugated epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 4 residues of the HBc sequence of positions 76 through 85 are present.

45. (original) The recombinant HBc chimer protein molecule according to claim 44 wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said heterologous linker residue for a conjugated epitope.

46. (original) The recombinant HBc chimer protein molecule according to claim 25 wherein the residue substituted for each cysteine at positions 48 and 107 is individually selected from the group consisting of glutamine, asparagine, serine, alanine, threonine and lysine.

47. (currently amended) A recombinant chimer hepatitis B core (HBc) protein molecule up to about 600 amino acid residues in length that

(a) contains an HBc sequence of at least about 125 of the N-terminal 183 amino acid residues of the HBc molecule that includes the HBc sequence of residue positions 4 through about 75 and about 85 through about 140 in which one or both cysteine residues at positions 48 and 107 is replaced by another residue, and in which the cysteine at residue position 61 is present;

(b) contains a peptide-bonded heterologous amino acid residue sequence at one or more of the N-terminus, in the HBc immunodominant loop between residue positions about 76 through about 85, and the HBc residue at each of positions 76 and 82 is replaced by a cysteine residue, or the C-terminus of the chimer, and wherein

[(i)] (1) zero to all residues in a sequence in said HBc immunodominant loop other than at position s 76 and 82 are present or replaced and said heterologous amino acid residue sequence comprises one to about 245 amino acid residues that constitute an immunogen or a sequence of 1 to about 40 residues that constitutes an anti-antigen or a chemically-reactive linker residue for a conjugated hapten; or

[(ii)] (2) one or more of residues 76 through 85 other than the cysteines at positions 76 and 82 is absent or replaced;

(c) contains one or both of

[(i)] (1) one to three cysteine residues at an amino acid position of the chimer molecule corresponding to amino acid position -20 to about +1 from the N-terminus of the HBc sequence of SEQ ID NO:1 [N-terminal cysteine residue(s)] in a sequence other than that of the HBc precore sequence and

[(ii)] (2) one to three cysteine residues toward the C-terminus of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule [C-terminal cysteine residue(s)]; said chimer molecule

(i) containing up to about 5 percent substituted amino acid residues in the HBc sequence relative to SEQ ID NO:1, and

(ii) self-assembling into particles that exhibit a ratio of absorbance at 280 nm to 260 nm of about 0.9 to about 1.7 after expression.